

Self guided Tour

REAXYS MEDICINAL CHEMISTRY

“WHAT IS KNOWN ABOUT MY SUBSTANCE OF INTEREST?”

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<http://beta.reaxys.com>

 **REAXYS**[®]
Medicinal Chemistry

WHAT IS KNOWN ABOUT MY SUBSTANCE OF INTEREST?

1.1 Scenario

An Apoptosis inducer 'chemotype' from a cell- and caspase-based apoptosis high-throughput screening was found (Compound 1). A structure activity relationship expansion lead to compound 2 (Schema1)

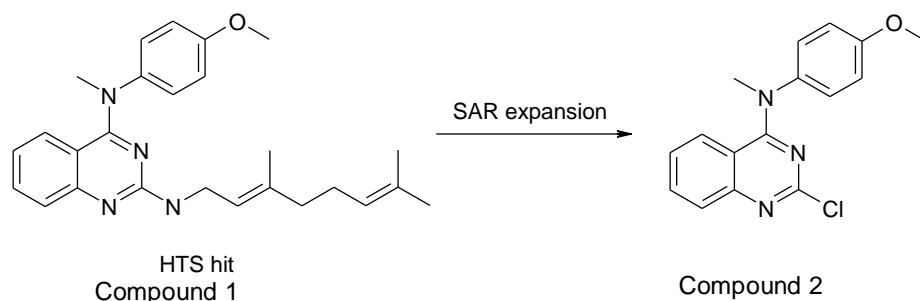


Figure 1 : Apoptosis inducer : From HTS hit to new chemotype

What is known about this chemotype/template (Compound 2) in Reaxys Medicinal Chemistry?

1.2 Overview

Step no.	Steps and description	Action
1	Search By Substances	Click on substance button
2	Draw your Substance	Use Marvin Sketch and draw structure
3	Search by Exact structure (default)	Click on Search Substances
4	"Substance Report" will display corresponding bioactivities	View default tab 'Substance Report'
5	"Bioactivity" link will display details on bioactivity categories	Check 'Bioactivity' link
6	Click on Bioactivity categories, it will display more details (biological results)	Check the three Bioactivity categories (In vivo, Pharmacokinetics, Toxicity)
7	Click on the bioactivities tab, it will display Substance and corresponding Targets (default view)	Click on 'Bioactivities' tab
8	Click on Axis values to change the heatmap view (cell lines instead of targets)	Click on Target X axis and change target to Cell lines in the popup
9	Click the Targets Tab	Click on 'Targets' tab
10	Click Show details in the target tab to know more about (Bioassays and cells lines)	Click on 'Show details' & Associated links under 'Show details'

1.3 Step by step

Query Results Synthesis Plans History Report My Alerts My Settings Help Live Chat Logout

Ask Reaxys Enter a keyword, concept or author Go

Examples

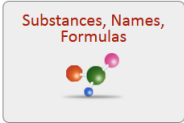
Find substances, reactions, bioactivity data, citations, patents, and more from Reaxys, PubChem, and eMolecules

Reactions Substances, Names, Formulas Medicinal Chemistry Literature ReaxysTree

You can also search directly by these common property groups:

Physical Spectra Natural Product Advanced


Step 1 Search By substances and Chemical drawing

Step	Action	Comment
1	Click on Substances, Names and Formulas Button 	A new query Page dedicated to Substance will appear where you will be able to draw Compound 2
2	Draw the chemical compound 2 or copy Smile (See remark below) and paste the smile and Select As Drawn in the option on the right	Don't forget to transfer the query before closing the sketcher

Remark : In order to save time for drawing the compound use the “Create structure Template for Name” and paste the following Smile.

Smile : COC1=CC=C(C=C1)N(C)C1=NC(Cl)=NC2=C1C=CC=C2

selected query editor:

 MarvinSketch
by ChemAxon

STRUCTURE EDITOR

Create Structure Template from Name

Step 2 : Search by Exact structure

Structure

As drawn
Substructure
on heteroatoms
on all atoms
Similarity

Include tautomers
Ignore stereo
No salts
No mixtures
No isotopes
No charges
No radicals
No ring closures
Align results with query

More options

Identification

Reaxys Registry Number = Lookup X

CAS Registry Number is Lookup X

Chemical Name is Lookup X

Element Symbols is Lookup X

Show AND Buttons

Add to Query: Structure Molecular Formula Alloy Add/Remove Fields... Search Substances

Step 3: Found Bioactivities of compound 2

Query Results Synthesis Plans History Report My Alerts My Settings Help Logout

Reaxys PubChem eMolecules

Query 3 substances

Create Alert

Open Analysis View

Filter by:

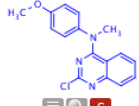
Bioactivities (44) Reactions (28) Substances (3) Targets (4) Citations (9) go to Page: 1 of 1

Structure	Structure/Compound Data	N° of preparations All Preps All Reactions	Available Data	Target	N° of ref.
	Chemical Name: EP128265 Reaxys Registry Number: 12173037 CAS Registry Number: 827030-33-1 Molecular Formula: C ₁₃ H ₁₄ ClN ₃ O Linear Structure Formula: C ₁₃ H ₁₄ ClN ₃ O Molecular Weight: 259.76 InChI Key: CIPVUQSDOVFBPO-UHFFFAOYSA-N Highest Clinical Phase: Preclinical	1 prep out of 10 reactions.	Druglikeness Bioactivity Identification Physical Data (1) Spectra (3)	Show Targets	7

Step 4: Click on Bioactivity to display all the available bioactivities by Categories

Bioactivities (44) Reactions (28) Substances (3) Targets (4) Citations (9) go to Page Page 1 of 1

Limit to Exclude Export Print Zoom in Zoom out Hide Sort by No of References Display as Exclude GoSTAR data

Structure	Structure/Compound Data	N° of preparations All Preps All Reactions	Available Data	Target	N° of ref.
 <p>Synthesize Hide Details Find similar</p>	<p>Chemical Name: EP128265</p> <p>Reaxys Registry Number: 12173037 CAS Registry Number: 827030-33-1 Molecular Formula: C₁₆H₁₄ClN₃O Linear Structure Formula: C₁₆H₁₄ClN₃O Molecular Weight: 299.76 InChI Key: CIPVUQSDDVFBPO-UHFFFAOYSA-N</p> <p>Highest Clinical Phase: Preclinical</p>	1 prep out of 10 reactions.	Druglikeness Bioactivity Identification Physical Data (1) Spectra (3)	Show Targets	7

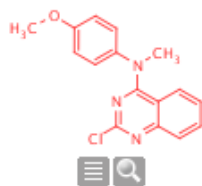
Chemical Names and Synonyms
EP128265, MPI-0441138, 2-chloro-N-(4-methoxyphenyl)-N-methylquinazolin-4-amine, (2-chloro-quinazolin-4-yl)-(4-methoxy-phenyl)-methyl-amine, (2-chloro-quinazolin-4-yl)-(4-methoxyphenyl)-methylamine

[Druglikeness](#)
[Bioactivity](#)
[In vitro: Efficacy \(27\)](#)
[In vivo: Animal Model \(1\)](#)
[Pharmacokinetic \(7\)](#)

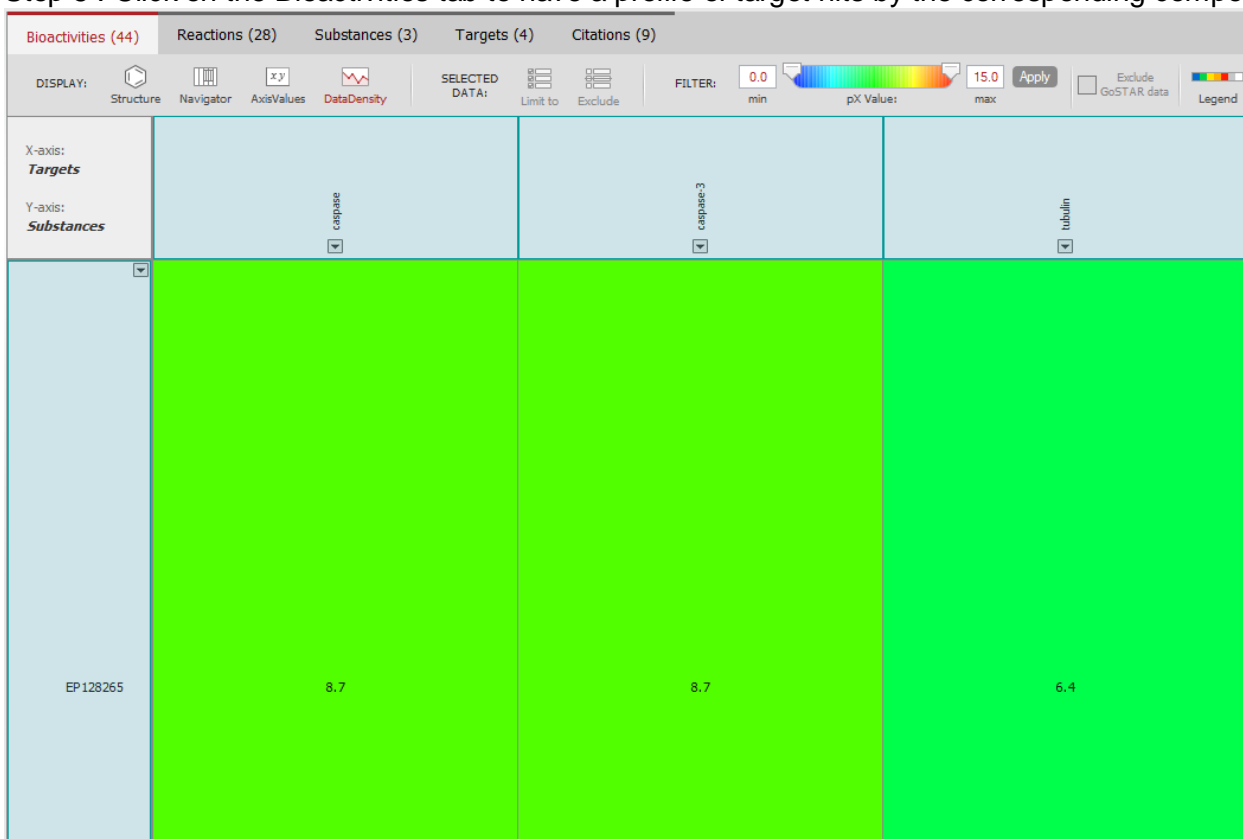
Quantitative Results

Parameter	Value (qual)	Value (quant)	Unit	Biological Species	Route of administration	Dose	Dosing regimen	Population	Reference (expand all/collapse all)
BB ratio		29.99		mouse	intravenous administration	0.875000 mg/mL	Single		Patent: WO2006/74187 A... Title/Abstract Full Text Show Details
AUC	=	20563	ng.h/mL	mouse	intravenous administration				Journal of Medicinal Che... Title/Abstract Full Text View citing articles Show Details
AUC	=	669	ng.h/mL	mouse	intravenous administration				Journal of Medicinal Che... Title/Abstract Full Text View citing articles Show Details
AUC	=	20563	ng.h/mL	mouse	intravenous administration				Journal of Medicinal Che... Title/Abstract Full Text View citing articles Show Details
AUC	=	669	ng/mL	mouse	intravenous administration				Journal of Medicinal Che... Title/Abstract Full Text View citing articles Show Details

Remark : The Hide Details Link will collapse all the bioactivity details

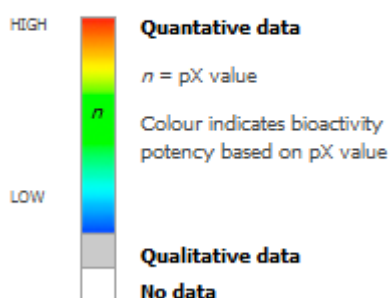


Step 5 : Click on the Bioactivities tab to have a profile of target hits by the corresponding compound



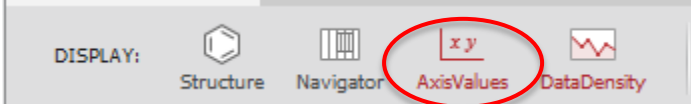
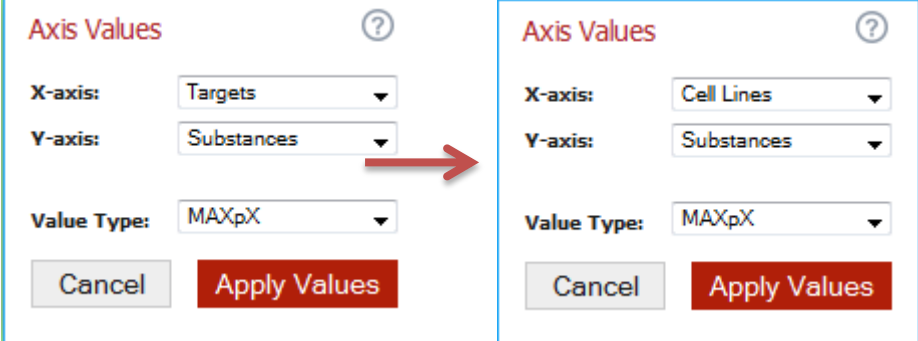
Color indicates bioactivity potency based on pX value. Number indicates pX value. (See legend Below)

Legend

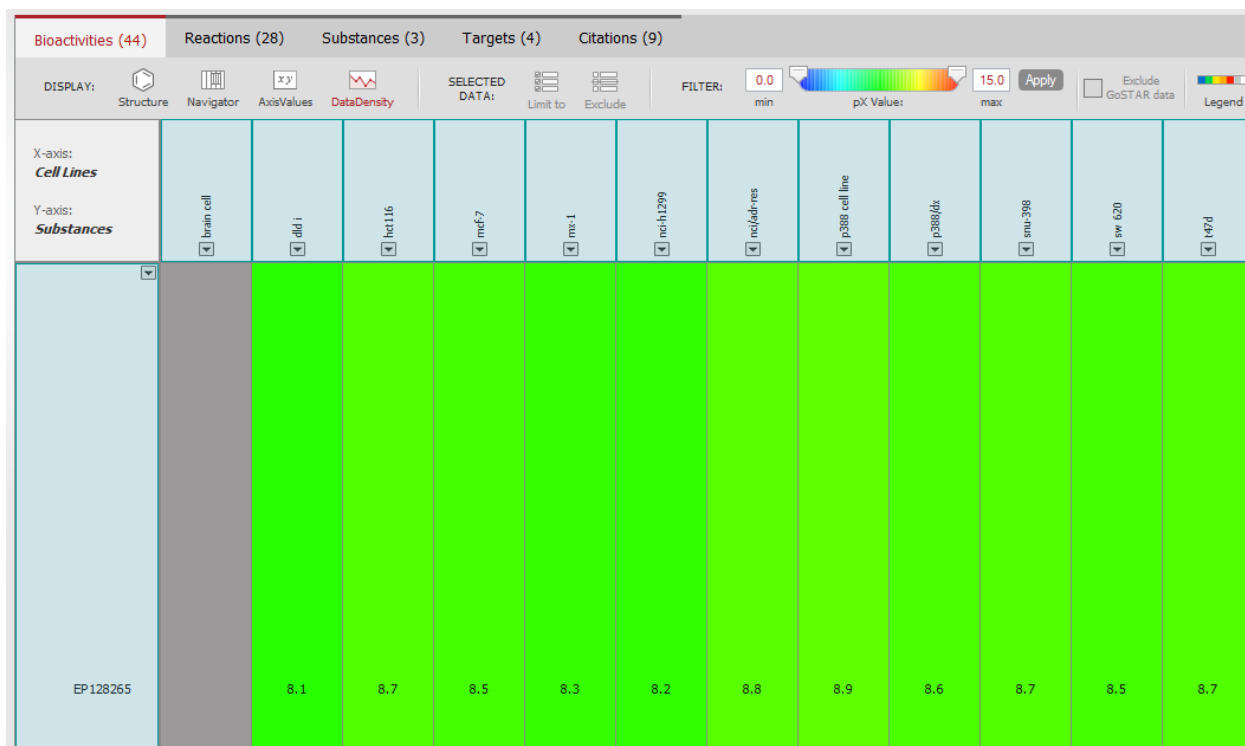


Step 6 : How to see the profile of compound 2 on Cell lines?

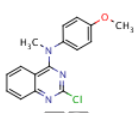
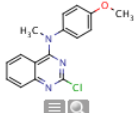
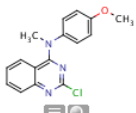
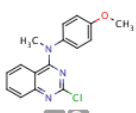
As we have seen before the compound 2 was also tested as antiproliferative agent on many cells lines how to see that using the bioactivities view?

Step	Action
1	Click on Axis Value 
2	Change X Axis from Target into Cell lines and click Apply 

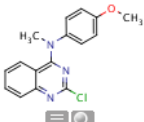
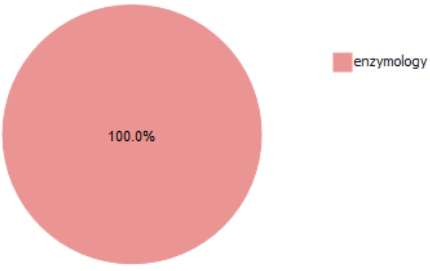
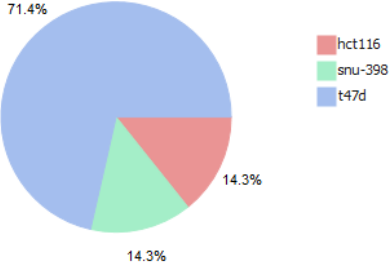
A profile on target will appear in the Bioactivities view.



Step 7 : Click the Targets Tab to have more details on targets on which this compound was tested (species etc....)

Bioactivities (44) Reactions (28) Substances (3) Targets (4) Citations (9)				
Limit to Exclude Export Print Zoom in Zoom out Hide Sort by Target Name <input type="checkbox"/> Exclude GoSTAR data				
Target	Target Details	Most active substance	Available Data	N° of ref.
1 Caspase Show Details	Species: Human Target type: Wild Protein Target Class: Caspase family (All)	 All substances	Bioactivities Associated Bioassays Associated Cells Ligand Bioactivities distribution	Show
2 Caspase Show Details	Target type: Wild Protein Target Class: Caspase family (All)	 EC50 = 2nM All substances	Bioactivities Associated Bioassays Associated Cells Ligand Bioactivities distribution	Show
3 Caspase-3 Show Details	Species: Human Target type: Wild Protein Target Class: Caspase family (All)	 EC50 = 2nM All substances	Bioactivities Associated Bioassays Associated Cells Ligand Bioactivities distribution	Show
4 Tubulin Show Details	Target type: Wild Protein Target Class: Other/Unclassified (All)	 IC50 = 400nM All substances	Bioactivities Associated Bioassays Associated Cells Ligand Bioactivities distribution	Show

Step 8 : To know which bioassays and/or Cells lines were used to generate the corresponding bioactivities on the caspase 3 click Show details

Caspase-3 Hide Details	Species: Human Target type: Wild Protein Target Class: Caspase family (All)	 EC50 = 2nM All substances	Bioactivities Associated Bioassays Associated Cells Ligand Bioactivities distribution	Show								
Associated Bioassays												
<p>Bioactivities distributed over Bioassays</p>  <table border="1"> <thead> <tr> <th>Bioassay Category</th> <th>Percentage</th> </tr> </thead> <tbody> <tr> <td>enzymology</td> <td>100.0%</td> </tr> </tbody> </table>					Bioassay Category	Percentage	enzymology	100.0%				
Bioassay Category	Percentage											
enzymology	100.0%											
Associated Cells												
<p>Bioactivities distributed over Cell Lines</p>  <table border="1"> <thead> <tr> <th>Cell Line</th> <th>Percentage</th> </tr> </thead> <tbody> <tr> <td>hct116</td> <td>14.3%</td> </tr> <tr> <td>snu-398</td> <td>14.3%</td> </tr> <tr> <td>t47d</td> <td>71.4%</td> </tr> </tbody> </table>					Cell Line	Percentage	hct116	14.3%	snu-398	14.3%	t47d	71.4%
Cell Line	Percentage											
hct116	14.3%											
snu-398	14.3%											
t47d	71.4%											

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